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EXAMINER	
POHNERT, STEVEN C	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Attachment to Advisory

Continuation of Box 3

The amendment to claims 1, 6, and 44, have added the limitation of "blood sample" to the independent claims. This amendment would require further search and consideration as it has moved the limitation from a dependent claim into an independent claim, thus requiring further consideration of dependent claims 74 (for claim 1), 12 and 13 (for claim 6), and 52 and 53 (for claim 44).

Continuation of box 11:

The response asserts on page 13 that the combination of all four was elected in response to restriction, the election does not require the loss of heterozygosity of the combination of all four markers. The examiner concurs with this interpretation. The claims require analyzing or detecting all four markers based on the election and making a determination based on the loss of any of the markers. The loss of any of the markers broadly encompasses loss of one, two, three or four of the markers.

The response asserts that APAF-1 expression does not specifically correlate with LOH of APAF1 as Soengas teaches in figures 1b and 1C samples 6 and 16 have LOH at one position and have APAF-1 expression by in situ hybridization. This argument has been thoroughly reviewed but is not considered persuasive as the claims are not drawn to LOH of APAF-1, but the loss of the elected markers. Thus these arguments are beyond the scope of the claimed invention.

The response further asserts that Soengas has mapped APAF-1 to a different position than the instant specification. This argument has been thoroughly reviewed but

is not considered persuasive as the claims are drawn to the detection of the elected markers. Thus these arguments are beyond the scope of the claimed invention.

The response continues by asserting that use of APAF-1 LOH to predict progression of melanoma would not allow for correct prediction. This argument has been thoroughly reviewed but is not considered persuasive as the claims are drawn to detecting the elected marker and use of the markers for determination of melanoma progression. Thus the arguments are beyond the scope of the claimed invention.

The response further asserts that Soengas fails to teach the loss of D12S1657, D12S393, D12S1706, or D12S346 with melanoma. This argument has been thoroughly reviewed but is not considered persuasive as the claims do not require the loss of any single marker as asserted, but the loss of any of the markers which includes the loss of one, two, three or four, which Soegnas teaches.

The response asserts that the combination of Soengas and Gocke do not render the instant claims 1-3, 6-8, 12-13, 74 and 81-81 obvious as neither teach detection of the elected markers in accellular DNA and accellular DNA analysis lack a reasonable expectation of success. This argument has been thoroughly reviewed but is not considered persuasive as Soengas teaches detection of the recited markers and Gocke teaches the use of accellular DNA for detection of disease. The detection of markers known to be associated with melanoma in accellular DNA that was known to be used for the detection of disease is the combination to two known technologies thus applying known techniques for analysis of known markers from known samples would allow for a reasonable expectation of success. The arguments to the unpredictability of accellular

DNA appears to be arguments of counsel not supported by evidence. First, MPEP 716.01(c) makes clear that "The arguments of counsel cannot take the place of evidence in the record. In re Schulze , 346 F.2d 600, 602, 145 USPQ 716, 718 (CCPA 1965). Examples of attorney statements which are not evidence and which must be supported by an appropriate affidavit or declaration include statements regarding unexpected results, commercial success, solution of a long - felt need, inoperability of the prior art, invention before the date of the reference, and allegations that the author(s) of the prior art derived the disclosed subject matter from the applicant." Here, the statements regarding unpredictability of accellular DNA must be supported by evidence, not argument.

This should not be construed as an invitation for providing evidence. As further stated in the MPEP 716.01 regarding the timely submission of evidence:

A) Timeliness.

Evidence traversing rejections must be timely or seasonably filed to be entered and entitled to consideration. In re Rothermel, 276 F.2d 393, 125 USPQ 328 (CCPA 1960). Affidavits and declarations submitted under 37 CFR 1.132 and other evidence traversing rejections are considered timely if submitted:

(1) prior to a final rejection,

(2) before appeal in an application not having a final rejection, or

(3) after final rejection and submitted

(i) with a first reply after final rejection for the purpose of overcoming a new ground of rejection or requirement made in the final rejection, or

(ii) with a satisfactory showing under 37 CFR 1.116(b) or 37

CFR 1.195, or

(iii) under 37 CFR 1.129(a).

With respect to claims 35 and 58-59 applicant again argues the teachings of Soengas are drawn to APAF-1 negative cells while the instant invention is drawn to LOH of any of the four markers. This argument has been thoroughly reviewed but is not considered persuasive as the claims require loss of one, two, three or four of the markers not determination based on the loss of a single one as the response appears to be asserting.

The response continues by asserting that the teachings of Soengas are in vitro and thus cannot render in vivo biochemotherapy as obvious. This is arguments of counsel that have not been supported by evidence. Based on the teachings of Soengas association of APAF-1 status with LOH of the elected combination of markers would render the instant claims obvious as Soengas teaches, "Assessment of APAF-1 status may therefore improve the therapeutic management of patients with malignant melanoma" (page 210, 2nd column, 1st paragraph). The direction by Soengas as to the LOH and therapeutic management of patients suggest the use of LOH of the elected marker in patients as a marker of chemo resistance, thus it would have been obvious to try. As there is no evidence to the unpredictability of the LOH of the elected marker in vitro versus in vivo the artisan would be motivated to try based on Soegnas direction.

The response asserts the teachings of Soengas to APAF-1 does not render the instant claims 44-45 obvious as the response asserts that Soengas does not teach loss

of one of D12S1657, D12S393, D12S1706, or D12S346 with low probability of survival. Soengas does suggest that LOH of the markers is indicative of decreased APAF-1 expression and thus indicative of progression and resistance to chemotherapy rendering the claims obvious. The response further asserts the teachings of Taback do not render the instant claims obvious. These arguments have been thoroughly reviewed but are not considered persuasive as the Soengas teaches the markers of he claims and Taback teaches LOH in blood as a prognostic indicator of metastatic melanoma, thus in combination with the teachings of Soengas renders the instant claims obvious.

Conclusions

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Steven C. Pohnert whose telephone number is (571)272-3803. The examiner can normally be reached on Monday-Friday 6:30-4:00, every second Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James (Doug) Schultz can be reached on 571-272-0763. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.